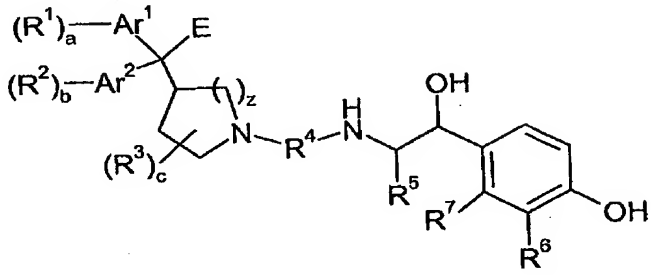
II. AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in this application.

1. (Original) A compound of formula I:



I

wherein:

Ar^1 represents phenyl, (3-6C)cycloalkyl, (3-5C)heteroaryl or (3-5C)heterocyclyl; wherein the heteroaryl and heterocyclyl groups contain 1 or 2 ring heteroatoms selected independently from oxygen, nitrogen and sulfur;

a is 0 or an integer from 1 to 3;

each R^1 is selected independently from (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, $-OR^{1a}$, $-SR^{1b}$, $-S(O)R^{1c}$, $-S(O)_2R^{1d}$, $-NR^{1e}R^{1f}$ and $-C(O)OR^{1g}$; or two adjacent R^1 groups are joined together to form (3-6C)alkylene, (2-4C)alkylene-O- or -O-(1-4C)alkylene)-O-;

each of R^{1a}, R^{1b}, R^{1c}, R^{1d}, R^{1e}, R^{1f} and R^{1g} is independently hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl;

Ar^2 represents phenyl, (3-6C)cycloalkyl, (3-5C)heteroaryl or (3-5C)heterocyclyl; wherein the heteroaryl and heterocyclyl group contain 1 or 2 ring heteroatoms selected independently from oxygen, nitrogen and sulfur;

b is 0 or an integer of from 1 to 3;

each R^2 is selected independently from (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, $-OR^{2a}$, $-SR^{2b}$, $-S(O)R^{2c}$, $-S(O)_2R^{2d}$, $-NR^{2e}R^{2f}$ and $-C(O)OR^{2g}$; or two adjacent R^2 groups are joined together to form (3-6C)alkylene, (2-4C)alkylene-O- or -O-(1-4C)alkylene)-O-;

each of R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{2e}, R^{2f} and R^{2g} is independently hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl;

E is –CN, -OH, $-C(O)NW^aW^b$ or $-C(O)OW^c$;

W^a and W^b are selected independently from hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl, or together with the nitrogen atom to which they are attached, W^a and W^b form a pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, morpholin-4-yl or thiomorpholin-4-yl group; or W^a and one R^1 are joined to form a covalent bond;

W^c is hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl;

c is 0 or an integer of from 1 to 4;

each R^3 is independently selected from (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, $-OR^{3a}$, $-SR^{3b}$, $-S(O)R^{3c}$, $-S(O)_2R^{3d}$ and $-NR^{3e}R^{3f}$ and $-C(O)OR^{3g}$; or two R^3 groups are joined to form (1-3C)alkylene, (2-3C)alkenylene or oxiran-2,3-diyl;

each of R^{3a}, R^{3b}, R^{3c}, R^{3d}, R^{3e}, R^{3f} and R^{3g} is independently hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl;

z is 1 or 2;

R^4 is a divalent group of the formula:

$$-(R^{4a})_d-(A^1)_e-(R^{4b})_f-Q-(R^{4c})_g-(A^2)_h-(R^{4d})_i-$$

wherein

d, e, f, g, h and i are each independently selected from 0 and 1;

R^{4a}, R^{4b}, R^{4c} and R^{4d} are each independently selected from (1-10C)alkylene, (2-10C)alkenylene and (2-10C)alkynylene, wherein each alkylene, alkenylene or alkynylene group is unsubstituted or substituted with from 1 to 5 substituents independently selected from (1-4C)alkyl, fluoro, hydroxy, phenyl and phenyl-(1-4C)alkyl;

A^1 and A^2 are each independently selected from (3-7C)cycloalkylene, (6-10C)arylene, -O-(6-10C)arylene, (6-10C)arylene-O-, (2-9C)heteroarylene, -O-(2-9C)heteroarylene, (2-9C)heteroarylene-O- and (3-6C)heterocyclene, wherein each cycloalkylene is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl, and each arylene, heteroarylene or heterocyclene group is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, $-S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy;

Q is selected from a bond, -O-, -C(O)O-, -OC(O)-, -S-, -S(O)-, $-S(O)_2$-, $-N(Q^a)C(O)$-, $-C(O)N(Q^b)$-, $-N(Q^c)S(O)_2$-, $-S(O)_2N(Q^d)$-, $-N(Q^e)C(O)N(Q^f)$-, $-N(Q^g)S(O)_2N(Q^h)$-, $-OC(O)N(Q^i)$-, $-N(Q^j)C(O)O$- and $-N(Q^k)$;

Q^a, Q^b, Q^c, Q^d, Q^e, Q^f, Q^g, Q^h, Q^i, Q^j and Q^k are each independently selected from hydrogen, (1-6C)alkyl, A^3 and (1-4C)alkylene-A^4, wherein the alkyl group is unsubstituted or substituted with from 1 to 3 substituents independently selected from fluoro, hydroxy and (1-4C)alkoxy; or together with the nitrogen atom and the group R^{4b} or R^{4c} to which they are attached, form a 4-6 membered azacycloalkylene group;

A^3 and A^4 are each independently selected from (3-6C)cycloalkyl, (6-10C)aryl, (2-9C)heteroaryl and (3-6C)heterocyclyl, wherein each cycloalkyl is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl and each aryl, heteroaryl or heterocyclyl group is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl and (1-4C)alkoxy;

provided that the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is in the range of from 4 to 16;

R^5 represents hydrogen or (1-4C)alkyl;

R^6 is $-NR^{6a}CR^{6b}(O)$ or $-CR^{6c}R^{6d}OR^{6e}$ and R^7 is hydrogen; or R^6 and R^7 together form $-NR^{7a}C(O)-CR^{7b}=CR^{7c}$-, $-CR^{7d}=CR^{7e}-C(O)-NR^{7f}$-, $-NR^{7g}C(O)-CR^{7h}R^{7i}-CR^{7j}R^{7k}$- or $-CR^{7l}R^{7m}-CR^{7n}R^{7o}-C(O)-NR^{7p}$-;

each of R^{6a}, R^{6b}, R^{6c}, R^{6d} and R^{6e} is independently hydrogen or (1-4C)alkyl; and

each of R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{7g}, R^{7h}, R^{7i}, R^{7j}, R^{7k}, R^{7l}, R^{7m}, R^{7n}, R^{7o} and R^{7p} is independently hydrogen or (1-4C)alkyl;

wherein each alkyl, alkenyl, alkylene and cycloalkyl group in R^1, R^{1a-g}, R^2, R^{2a-g}, R^3, R^{3a-g}, W^{a-c} is optionally substituted with from 1 to 5 fluoro substituents;

or a pharmaceutically acceptable salt or solvate or stereoisomer thereof.

2. (Original) The compound of Claim 1, wherein the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is in the range of from 8 to 14.

3. (Original) The compound of Claim 2, wherein the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is 8, 9, 10 or 11.

4. (Original) The compound of Claim 1, wherein Ar^1 and Ar^2 independently represent phenyl, (3-6C)cycloalkyl or (3-5C)heteroaryl.

5. (Original) The compound of Claim 4, wherein Ar^1 and Ar^2 are independently selected from phenyl, pyridyl, thienyl, cyclobutyl, cyclopentyl or cyclohexyl.

6. (Original) The compound of Claim 5, wherein Ar^1 and Ar^2 are both phenyl.

7. (Original) The compound of Claim 1, wherein a, b and c are 0.

8. (Original) The compound of Claim 1, wherein E is $-C(O)NW^aW^b$.

9. (Original) The compound of Claim 8, wherein E is $-C(O)NH_2$.

10. (Original) The compound of Claim 1, wherein z is 1.

11. (Original) The compound of Claim 1, wherein R^6 is -NHCHO or $-CH_2OH$ and R^7 is hydrogen; or R^6 and R^7 together form $-NHC(O)-CH=CH-$, $-CH=CH-C(O)-NH-$, $-CH_2-CH_2-C(O)NH-$ or $-NHC(O)-CH_2-CH_2-$.

12. (Original) The compound of Claim 1, wherein R^4 is a divalent group of the formula: $-(R^{4a})_d-$ where R^{4a} is (4-10C)alkylene.

13. (Original) The compound of Claim 12, wherein R^4 is $-(CH_2)_8-$, $-(CH_2)_9$, and $-(CH_2)_{10}-$.

14. (Original) The compound of Claim 1, wherein R^4 is a divalent group of the formula:

$$-(R^{4a})_d-(A^2)_h-(R^{4d})_i-$$

wherein R^{4a} is (1-10C)alkylene; A^2 is (6-10C)arylene or (2-9C)heteroarylene; and R^{4d} is (1-10C)alkylene.

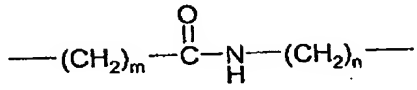
15. (Original) The compound of Claim 1, wherein R^4 is a divalent group of the formula:

$$-(R^{4a})_d-Q-(A^2)_h-(R^{4d})_i-$$

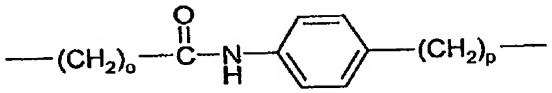
wherein Q is -O- or $-N(Q^k)-$; Q^k is hydrogen or (1-3C)alkyl; R^{4a} is (1-10C)alkylene; A^2 is (6-10C)arylene or (2-9C)heteroarylene; and R^{4d} is (1-10C)alkylene.

16. (Original) The compound of Claim 1, wherein Q is $-N(Q^a)C(O)-$ or $-C(O)N(Q^b)-$.

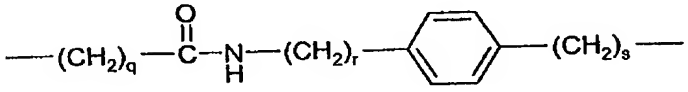
17. (Original) The compound of Claim 16, wherein R^4 is selected from:



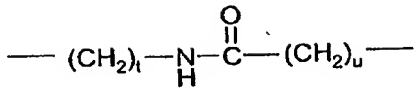
wherein m is an integer from 2 to 10; and n is an integer from 2 to 10; provided that m + n is an integer from 4 to 12;



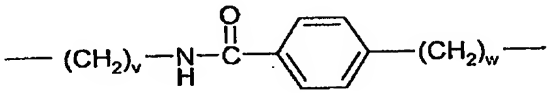
wherein o is an integer from 2 to 7; and p is an integer from 1 to 6; provided that o + p is an integer from 3 to 8; and wherein the phen-1,4-ylene group is optionally substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -$S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy;



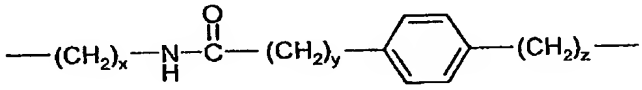
wherein q is an integer from 2 to 6; r is an integer from 1 to 5; and s is an integer from 1 to 5; provided that q + r + s is an integer from 4 to 8; and wherein the phen-1,4-ylene group is optionally substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -$S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy;



wherein t is an integer from 2 to 10; and u is an integer from 2 to 10; provided that t + u is an integer from 4 to 12;

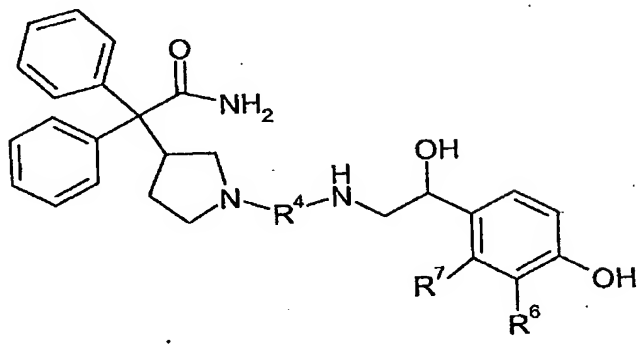


wherein v is an integer from 2 to 7; and w is an integer from 1 to 6; provided that v + w is an integer from 3 to 8; and wherein the phen-1,4-ylene group is optionally substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -$S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy; and



wherein x is an integer from 2 to 6; y is an integer from 1 to 5; and z is an integer from 1 to 5; provided that x + y + z is an integer from 4 to 8; and wherein the phen-1,4-ylene group is optionally substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -$S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy.

18. (Original) A compound of formula II:



II

wherein

R^4 is a divalent group of the formula:

$$-(R^{4a})_d-(A^1)_e-(R^{4b})_f-Q-(R^{4c})_g-(A^2)_h-(R^{4d})_i-$$

wherein

d, e, f, g, h and i are each independently selected from 0 and 1;

R^{4a}, R^{4b}, R^{4c} and R^{4d} are each independently selected from (1-10C)alkylene, (2-10C)alkenylene and (2-10C)alkynylene, wherein each alkylene, alkenylene or alkynylene group is unsubstituted or substituted with from 1 to 5 substituents independently selected from (1-4C)alkyl, fluoro, hydroxy, phenyl and phenyl-(1-4C)alkyl;

A^1 and A^2 are each independently selected from (3-7C)cycloalkylene, (6-10C)arylene, -O-(6-10C)arylene, (6-10C)arylene-O-, (2-9C)heteroarylene, -O-(2-9C)heteroarylene, (2-9C)heteroarylene-O- and (3-6C)heterocyclene, wherein each cycloalkylene is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl, and each arylene, heteroarylene or heterocyclene group is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -$S(O)_2$-(1-4C)alkyl,

-C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy;

Q is selected from a bond, -O-, -C(O)O-, -OC(O)-, -S-, -S(O)-, -$S(O)_2$-, -$N(Q^a)C(O)$-, -$C(O)N(Q^b)$-, -$N(Q^c)S(O)_2$-, -$S(O)_2N(Q^d)$-, -$N(Q^e)C(O)N(Q^f)$-, -$N(Q^g)S(O)_2N(Q^h)$-, -$OC(O)N(Q^i)$-, -$N(Q^j)C(O)O$- and –$N(Q^k)$;

Q^a, Q^b, Q^c, Q^d, Q^e, Q^f, Q^g, Q^h, Q^i, Q^j and Q^k are each independently selected from hydrogen, (1-6C)alkyl, A^3 and (1-4C)alkylene-A^4, wherein the alkyl group is unsubstituted or substituted with from 1 to 3 substituents independently selected from fluoro, hydroxy and (1-4C)alkoxy; or together with the nitrogen atom and the group R^{4b} or R^{4c} to which they are attached, form a 4-6 membered azacycloalkylene group;

A^3 and A^4 are each independently selected from (3-6C)cycloalkyl, (6-10C)aryl, (2-9C)heteroaryl and (3-6C)heterocyclyl, wherein each cycloalkyl is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl and each aryl, heteroaryl or heterocyclyl group is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl and (1-4C)alkoxy;

provided that the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is in the range of from 4 to 16;

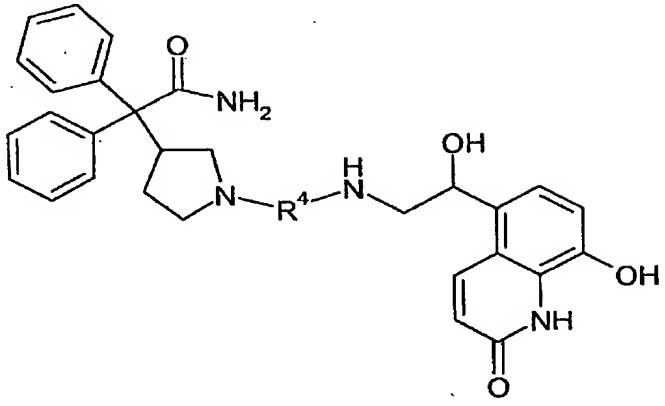
R^6 is -$NR^{6a}CR^{6b}(O)$ or -$CR^{6c}R^{6d}OR^{6e}$ and R^7 is hydrogen; or R^6 and R^7 together form -$NR^{7a}C(O)$-CR^{7b}=CR^{7c}-, -CR^{7d}=CR^{7e}-C(O)-NR^{7f}-, -$NR^{7g}C(O)$-$CR^{7h}R^{7i}$-$CR^{7j}R^{7k}$- or -$CR^{7l}R^{7m}$-$CR^{7n}R^{7o}$- C(O) -NR^{7p}-;

each of R^{6a}, R^{6b}, R^{6c}, R^{6d} and R^{6e} is independently hydrogen or (1-4C)alkyl; and

each of R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{7g}, R^{7h}, R^{7i}, R^{7j}, R^{7k}, R^{7l}, R^{7m}, R^{7n}, R^{7o} and R^{7p} is independently hydrogen or (1-4C)alkyl;

or a pharmaceutically acceptable salt or solvate or stereoisomer thereof.

19. (Original) A compound of formula III:



III

wherein

R^4 is a divalent group of the formula:

$$-(R^{4a})_d-(A^1)_e-(R^{4b})_f-Q-(R^{4c})_g-(A^2)_h-(R^{4d})_i-$$

wherein

d, e, f, g, h and i are each independently selected from 0 and 1;

R^{4a}, R^{4b}, R^{4c} and R^{4d} are each independently selected from (1-10C)alkylene, (2-10C)alkenylene and (2-10C)alkynylene, wherein each alkylene, alkenylene or alkynylene group is unsubstituted or substituted with from 1 to 5 substituents independently selected from (1-4C)alkyl, fluoro, hydroxy, phenyl and phenyl-(1-4C)alkyl;

A^1 and A^2 are each independently selected from (3-7C)cycloalkylene, (6-10C)arylene, -O-(6-10C)arylene, (6-10C)arylene-O-, (2-9C)heteroarylene, -O-(2-9C)heteroarylene, (2-9C)heteroarylene-O- and (3-6C)heterocyclene, wherein each cycloalkylene is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl, and each arylene, heteroarylene or heterocyclene group

is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, $-S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy;

Q is selected from a bond, -O-, -C(O)O-, -OC(O)-, -S-, -S(O)-, $-S(O)_2$-, $-N(Q^a)C(O)-$, $-C(O)N(Q^b)-$, $-N(Q^c)S(O)_2-$, $-S(O)_2N(Q^d)-$, $-N(Q^e)C(O)N(Q^f)-$, $-N(Q^g)S(O)_2N(Q^h)-$, $-OC(O)N(Q^i)-$, $-N(Q^j)C(O)O-$ and $-N(Q^k)$;

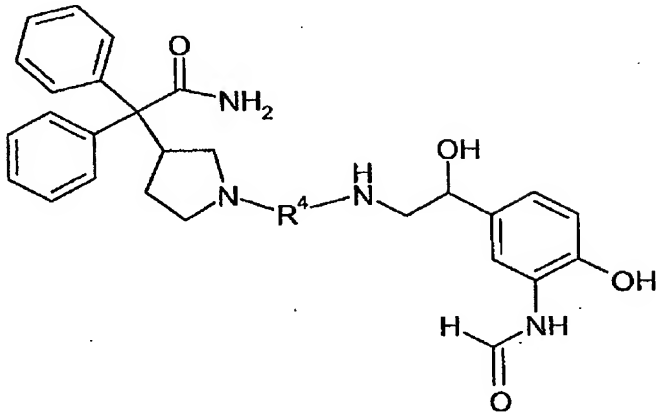
Q^a, Q^b, Q^c, Q^d, Q^e, Q^f, Q^g, Q^h, Q^i, Q^j and Q^k are each independently selected from hydrogen, (1-6C)alkyl, A^3 and (1-4C)alkylene-A^4, wherein the alkyl group is unsubstituted or substituted with from 1 to 3 substituents independently selected from fluoro, hydroxy and (1-4C)alkoxy; or together with the nitrogen atom and the group R^{4b} or R^{4c} to which they are attached, form a 4-6 membered azacycloalkylene group;

A^3 and A^4 are each independently selected from (3-6C)cycloalkyl, (6-10C)aryl, (2-9C)heteroaryl and (3-6C)heterocyclyl, wherein each cycloalkyl is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl and each aryl, heteroaryl or heterocyclyl group is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl and (1-4C)alkoxy;

provided that the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is in the range of from 4 to 16;

or a pharmaceutically acceptable salt or solvate or stereoisomer thereof.

20. (Original) A compound of formula IV:



IV

wherein

R^4 is a divalent group of the formula:

$$-(R^{4a})_d-(A^1)_e-(R^{4b})_f-Q-(R^{4c})_g-(A^2)_h-(R^{4d})_i-$$

wherein

d, e, f, g, h and i are each independently selected from 0 and 1;

R^{4a}, R^{4b}, R^{4c} and R^{4d} are each independently selected from (1-10C)alkylene, (2-10C)alkenylene and (2-10C)alkynylene, wherein each alkylene, alkenylene or alkynylene group is unsubstituted or substituted with from 1 to 5 substituents independently selected from (1-4C)alkyl, fluoro, hydroxy, phenyl and phenyl-(1-4C)alkyl;

A^1 and A^2 are each independently selected from (3-7C)cycloalkylene, (6-10C)arylene, -O-(6-10C)arylene, (6-10C)arylene-O-, (2-9C)heteroarylene, -O-(2-9C)heteroarylene, (2-9C)heteroarylene-O- and (3-6C)heterocyclene, wherein each cycloalkylene is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl, and each arylene, heteroarylene or heterocyclene group

is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -$S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy;

Q is selected from a bond, -O-, -C(O)O-, -OC(O)-, -S-, -S(O)-, -$S(O)_2$-, -$N(Q^a)C(O)$-, -$C(O)N(Q^b)$-, -$N(Q^c)S(O)_2$-, -$S(O)_2N(Q^d)$-, -$N(Q^e)C(O)N(Q^f)$-, -$N(Q^g)S(O)_2N(Q^h)$-, -$OC(O)N(Q^i)$-, -$N(Q^j)C(O)O$- and –$N(Q^k)$;

Q^a, Q^b, Q^c, Q^d, Q^e, Q^f, Q^g, Q^h, Q^i, Q^j and Q^k are each independently selected from hydrogen, (1-6C)alkyl, A^3 and (1-4C)alkylene-A^4, wherein the alkyl group is unsubstituted or substituted with from 1 to 3 substituents independently selected from fluoro, hydroxy and (1-4C)alkoxy; or together with the nitrogen atom and the group R^{4b} or R^{4c} to which they are attached, form a 4-6 membered azacycloalkylene group;

A^3 and A^4 are each independently selected from (3-6C)cycloalkyl, (6-10C)aryl, (2-9C)heteroaryl and (3-6C)heterocyclyl, wherein each cycloalkyl is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl and each aryl, heteroaryl or heterocyclyl group is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl and (1-4C)alkoxy;

provided that the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is in the range of from 4 to 16;

or a pharmaceutically acceptable salt or solvate or stereoisomer thereof.

21. (Original) The compound of any one of Claims 18, 19 or 20, wherein the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is in the range of from 8 to 14.

22. (Original) The compound of any one of Claims 18, 19 or 20, wherein the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is 8, 9, 10 or 11.

23. (Original) The compound of any one of Claims 18, 19 or 20, wherein R^4 is a divalent group of the formula: $-(R^{4a})_d-$ where R^{4a} is (4-10C)alkylene.

24. (Original) The compound of Claim 23, wherein R^4 is $-(CH_2)_8-$, $-(CH_2)_9$, and $-(CH_2)_{10}-$.

25. (Original) The compound of any one of Claims 18, 19 or 20, wherein R^4 is a divalent group of the formula:

$$-(R^{4a})_d-(A^2)_h-(R^{4d})_i-$$

wherein R^{4a} is (1-10C)alkylene; A^2 is (6-10C)arylene or (2-9C)heteroarylene; and R^{4d} is (1-10C)alkylene.

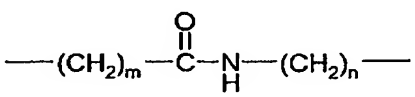
26. (Original) The compound of any one of Claims 18, 19 or 20, wherein R^4 is a divalent group of the formula:

$$-(R^{4a})_d-Q-(A^2)_h-(R^{4d})_i-$$

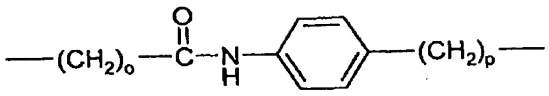
wherein Q is -O- or $-N(Q^k)-$; Q^k is hydrogen or (1-3C)alkyl; R^{4a} is (1-10C)alkylene; A^2 is (6-10C)arylene or (2-9C)heteroarylene; and R^{4d} is (1-10C)alkylene.

27. (Original) The compound of any one of Claims 18, 19 or 20, wherein Q is $-N(Q^a)C(O)-$ or $-C(O)N(Q^b)-$.

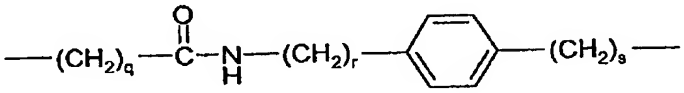
28. (Original) The compound of Claim 27 wherein R^4 is selected from:



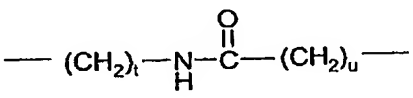
wherein m is an integer from 2 to 10; and n is an integer from 2 to 10; provided that m + n is an integer from 4 to 12;



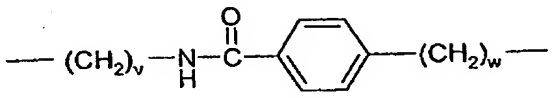
wherein o is an integer from 2 to 7; and p is an integer from 1 to 6; provided that o + p is an integer from 3 to 8; and wherein the phen-1,4-ylene group is optionally substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -$S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy;



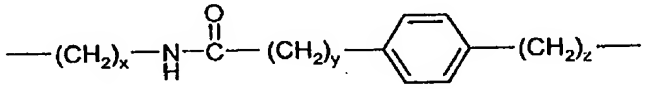
wherein q is an integer from 2 to 6; r is an integer from 1 to 5; and s is an integer from 1 to 5; provided that q + r + s is an integer from 4 to 8; and wherein the phen-1,4-ylene group is optionally substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -$S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy;



wherein t is an integer from 2 to 10; and u is an integer from 2 to 10; provided that t + u is an integer from 4 to 12;



wherein v is an integer from 2 to 7; and w is an integer from 1 to 6; provided that v + w is an integer from 3 to 8; and wherein the phen-1,4-ylene group is optionally substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -S(O)$_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy; and



wherein x is an integer from 2 to 6; y is an integer from 1 to 5; and z is an integer from 1 to 5; provided that x + y + z is an integer from 4 to 8; and wherein the phen-1,4-ylene group is optionally substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -S(O)$_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy.

29. (Original) The compound of any one of Claims 18, 19 or 20, wherein R^4 is selected from:

-$(CH_2)_7$-;

-$(CH_2)_8$-;

-$(CH_2)_9$-;

-$(CH_2)_{10}$-;

-$(CH_2)_{11}$-;

-$(CH_2)_2C(O)NH(CH_2)_5$-;

-$(CH_2)_2N(CH_3)C(O)(CH_2)_5$-;

-$(CH_2)_2C(O)NH$(phen-1,4-ylene)CH_2-;

-$(CH_2)_2NHC(O)$(phen-1,4-ylene)CH_2-;

-$(CH_2)_2NHC(O)NH(CH_2)_5$-;

-$(CH_2)_3NHC(O)NH(CH_2)_5$-;

-$(CH_2)_2C(O)NHCH_2$(cyclohex-1,3-ylene)CH_2-;

-$(CH_2)_2NHC(O)$(*cis*-cyclopent-1,3-ylene)-;

-$(CH_2)_2NHC(O)NH$(phen-1,4-ylene)$(CH_2)_2$-;

1-[-$(CH_2)_2C(O)$](piperidin-4-yl)$(CH_2)_2$-;

-$(CH_2)_2NHC(O)$(*trans*-cyclohex-1,4-ylene)CH_2-;

-$(CH_2)_2NHC(O)$(*cis*-cyclopent-1,3-ylene)-;

-$(CH_2)_2NH$(phen-1,4-ylene)$(CH_2)_2$-;

1-[-$(CH_2)_2NHC(O)$](piperidin-4-yl)$(CH_2)_2$-;

-CH_2(phen-1,4-ylene)NH(phen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NHCH_2$(phen-1,3-ylene)CH_2-;

-$(CH_2)_2C(O)NHCH_2$(pyrid-2,6-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(*cis*-cyclohex-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(*trans*-cyclohex-1,4-ylene)CH_2-;

-$(CH_2)_2NHC(O)$(*cis*-cyclopent-1,3-ylene)CH_2-;

-$(CH_2)_2N(CH_3)C(O)$(phen-1,3-ylene)CH_2-;

-$(CH_2)_2N(CH_3)C(O)$(*trans*-cyclohex-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(phen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(phen-1,4-ylene)C*H(CH_3)- ((*S*)-isomer);

-$(CH_2)_2C(O)NH$(phen-1,4-ylene)C*H(CH_3)- ((*R*)-isomer);

2-[(S)-(-CH_2-](pyrrolidin-1-yl)C(O)$(CH_2)_4$-;

2-[(S)-(-CH_2-](pyrrolidin-1-yl)C(O)(phen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(4-chlorophen-1,3-ylene)CH_2-;

-CH_2(2-fluorophen-1,3-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(4-methylphen-1,3-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(6-chlorophen-1,3-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(2-chlorophen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(2,6-dichlorophen-1,4-ylene)CH_2-;

-$(CH_2)_2NHC(O)NHCH_2$(phen-1,3-ylene)CH_2-;

4-[-CH_2-](piperidin-1-yl)C(O)(phen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)N(CH_2CH_3)$(phen-1,4-ylene)CH_2-;

1-[-$(CH_2)_2NHC(O)$](piperidin-4-yl)-;

-$(CH_2)_2C(O)NH$(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_2NHC(O)$(thien-2,5-ylene)CH_2-;

-$(CH_2)_2N(CH_3)C(O)$(3-nitrophen-1,4-ylene)CH_2-;

-$(CH_2)_2N(CH_3)C(O)$(*trans*-cyclohex-1,4-ylene)-;

1-[-CH_2(2-fluorophen-1,3-ylene)CH_2](piperidin-4-yl)-;

5-[-$(CH_2)_2NHC(O)$](pyrid-2-yl)CH_2-;

-$(CH_2)_2$(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_3$(thien-2,5-ylene)$(CH_2)_3$-;

-$(CH_2)_2$(phen-1,4-ylene)NH(phen-1,4-ylene)$(CH_2)_2$-;

-CH_2(phen-1,2-ylene)NH(phen-1,4-ylene)$(CH_2)_2$-;

1-[-CH_2(2-fluorophen-1,3-ylene)CH_2](piperidin-4-yl)$(CH_2)_2$-;

1-[-CH_2(2-fluorophen-1,3-ylene)CH_2](piperidin-4-yl)CH_2-;

-$(CH_2)_2C(O)NH$(3-chlorophen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(2-(CF_3O-)phen-1,4-ylene)CH_2-;

-$(CH_2)_3$(phen-1,3-ylene)NH(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_2S(O)_2NH(CH_2)_5$-;

-CH_2(phen-1,3-ylene)NH(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_2C(O)NH$(2-iodophen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(2-chloro-5-methoxyphen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(2-chloro-6-methylphen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH(CH_2)_5$-;

-$(CH_2)_2N(CH_3)S(O)_2$(phen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(2-bromophen-1,4-ylene)CH_2-;

-$(CH_2)_3$(phen-1,4-ylene)NH(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_3$(phen-1,2-ylene)NH(phen-1,4-ylene)$(CH_2)_2$-;

1-[-CH_2(2-fluorophen-1,3-ylene)CH_2](piperidin-4-yl)$(CH_2)_3$-;

-$(CH_2)_2C(O)NH$(2-methoxyphen-1,4-ylene)CH_2-;

-$(CH_2)_5NH$(phen-1,4-ylene)$(CH_2)_2$-;

4-[-$(CH_2)_2$-](piperidin-1-yl)(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_2C(O)NH$(phen-1,4-ylene)$CH(CH_3)CH_2$-;

-$(CH_2)_2$-(*trans*-cyclohex-1,4-ylene)NH(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_2C(O)NH$(2-fluorophen-1,4-ylene)CH_2-;

-$(CH_2)_2$(phen-1,3-ylene)NH(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_2C(O)NH$(2,5-difluorophen-1,4-ylene)CH_2-;

-$(CH_2)_2NHC(O)$(phen-1,4-ylene)$(CH_2)_2$-;

1-[-CH_2(pyrid-2,6-ylene)CH_2](piperidin-4-yl)CH_2-;

-$(CH_2)_3NH$(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_2NH$(naphth-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_3O$(phen-1,4-ylene)CH_2-;

1-[-$(CH_2)_3$](piperidin-4-yl)CH_2-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)(phen-1,4-ylene)CH_2-;

-$(CH_2)_3$(phen-1,4-ylene)NHC(O)$(CH_2)_2$-;

-$(CH_2)_3O$(phen-1,4-ylene)$(CH_2)_2$-;

2-[-$(CH_2)_2$](benzimidazol-5-yl)CH_2-;

-$(CH_2)_2$-(*trans*-cyclohex-1,4-ylene)NHC(O)$(CH_2)_2$-;

-$(CH_2)_2$-(*trans*-cyclohex-1,4-ylene)NHC(O)$(CH_2)_4$-;

-$(CH_2)_2$-(*trans*-cyclohex-1,4-ylene)NHC(O)$(CH_2)_5$-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)$(CH_2)_2$-;

-$(CH_2)_2NHC(O)NH$(phen-1,4-ylene)CH_2-;

-$(CH_2)_2N(CH_3)(CH_2)_2$(*cis*-cyclohex-1,4-ylene)-;

-$(CH_2)_2C(O)NH$(2,3,5,6-tetrafluorophen-1,4-ylene)CH_2-;

-$(CH_2)_2C(O)NH$(2,6-diiodophen-1,4-ylene)CH_2-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)$(CH_2)_3$-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)$(CH_2)_4$-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)$(CH_2)_5$-;

-$(CH_2)_2$C(O)NHCH_2(phen-1,4-ylene)CH_2-;

-$(CH_2)_2$NHC(O)NHCH_2(phen-1,4-ylene)CH_2-;

-$(CH_2)_2$C(O)NH(2-methylphen-1,4-ylene)CH_2-;

1-[-$(CH_2)_3$O(phen-1,4-ylene)$(CH_2)_2$](piperidin-4-yl)CH_2-;

-$(CH_2)_2$C(O)NHCH_2(phen-1,3-ylene)$(CH_2)_2$-;

-$(CH_2)_2$O(phen-1,3-ylene)CH_2-;

-$(CH_2)_2$N(CH_3)C(O)CH_2O(phen-1,4-ylene)CH_2-;

-$(CH_2)_2$N(CH_3)C(O)CH_2O(phen-1,3-ylene)CH_2-;

-$(CH_2)_2$N(CH_3)C(O)(fur-2,5-ylene)CH_2-;

-$(CH_2)_2$N(CH_3)C(O)(thien-2,5-ylene)CH_2-;

-$(CH_2)_2$O(phen-1,4-ylene)O$(CH_2)_2$-;

-$(CH_2)_2$(*trans*-cyclohex-1,4-ylene)NHC(O)(phen-1,4-ylene)CH_2-;

-$(CH_2)_2$(*trans*-cyclohex-1,4-ylene)NHC(O)CH_2O(phen-1,2-ylene)CH_2-;

-$(CH_2)_2$(*trans*-cyclohex-1,4-ylene)NHC(O)CH_2O(phen-1,3-ylene)CH_2-;

-$(CH_2)_2$(*trans*-cyclohex-1,4-ylene)NHC(O)CH_2O(phen-1,4-ylene)CH_2-;

-$(CH_2)_2$(*trans*-cyclohex-1,4-ylene)NHC(O)(fur-2,5-ylene)CH_2-;

-$(CH_2)_2$(*trans*-cyclohex-1,4-ylene)NHC(O)(thien-2,5-ylene)CH_2-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)CH_2O(phen-1,2-ylene)CH_2-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)CH_2O(phen-1,3-ylene)CH_2-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)CH_2O(phen-1,4-ylene)CH_2-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)(fur-2,5-ylene)CH_2-;

4-[-$(CH_2)_2$](piperidin-1-yl)C(O)(thien-2,5-ylene)CH_2-;

-$(CH_2)_2$(phen-1,4-ylene)NHC(O)(phen-1,3-ylene)CH_2-;

-$(CH_2)_2$(phen-1,4-ylene)NHC(O)(phen-1,4-ylene)CH_2-;

-$(CH_2)_2$(phen-1,4-ylene)NHC(O)CH_2O(phen-1,2-ylene)CH_2-;

-$(CH_2)_2$(phen-1,4-ylene)NHC(O)CH_2O(phen-1,3-ylene)CH_2-;

-$(CH_2)_2$(phen-1,4-ylene)NHC(O)CH_2O(phen-1,4-ylene)CH_2-;

-$(CH_2)_2$(phen-1,4-ylene)NHC(O)(fur-2,5-ylene)CH_2-;

-$(CH_2)_2$(phen-1,4-ylene)NHC(O)(thien-2,5-ylene)CH_2-;

-$(CH_2)_2$(*trans*-cyclohex-1,4-ylene)NHC(O)(phen-1,3-ylene)CH_2-;

-$(CH_2)_3$O(phen-1,3-ylene)CH_2-;

-$CH_2CH(OH)CH_2NH$(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_4NH$(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_2C(O)NH$(phen-1,4-ylene)$CH_2NHC(O)CH_2$-;

-$(CH_2)_2C(O)NH$(phen-1,4-ylene)$(CH_2)_2NHC(O)CH_2$-;

-$(CH_2)_2C(O)NHCH_2$(*trans*-cyclohex-1,4-ylene)CH_2-;

-$(CH_2)_2NHC(O)(CH_2)_5$-;

-$(CH_2)_2O$(phen-1,3-ylene)$O(CH_2)_2$-;

-$(CH_2)_2O$(phen-1,2-ylene)$O(CH_2)_2$-;

-CH_2(phen-1,2-ylene)O(phen-1,2-ylene)CH_2-;

-$(CH_2)_2C(O)NH(CH_2)_6$-;

-$(CH_2)_3$(phen-1,4-ylene)$(CH_2)_3$-;

-$(CH_2)_3$(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_4$(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_3$(furan-2,5-ylene)$(CH_2)_3$-;

-$(CH_2)_2N(CH_3)C(O)NH$(phen-1,4-ylene)$(CH_2)_2$-;

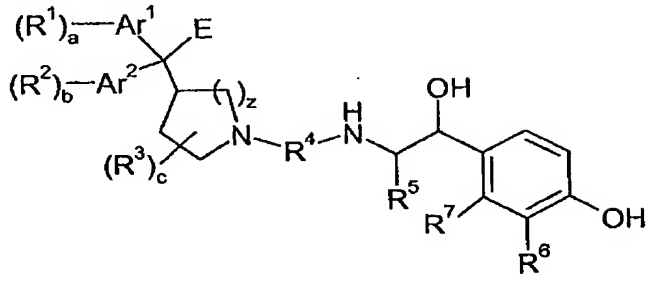
4-[-$(CH_2)_2$](piperidin-1-yl)C(O)NH(phen-1,4-ylene)$(CH_2)_2$-;

-$(CH_2)_3$(phen-1,3-ylene)$(CH_2)_3$-;

-$(CH_2)_3$(tetrahydrofuran-2,5-ylene)$(CH_2)_3$-; and

-$(CH_2)_2O$(phen-1,4-ylene)$C(O)(CH_2)_2$-.

30. (Original) A compound of formula I:



I

wherein:

Ar^1 represents a phenyl, (5-6C)cycloalkyl, (4-5C)heteroaryl or (4-5C)heterocyclyl group wherein the (4-5C)heteroaryl or (4-5C)heterocyclyl group contains one ring heteroatom selected from oxygen, nitrogen and sulfur;

each R^1 represents an optional substituent on Ar^1 that is independently selected from the group consisting of (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, $-OR^{1a}$, $-SR^{1b}$, $-S(O)R^{1c}$, $-S(O)_2R^{1d}$, and $-NR^{1e}R^{1f}$; or two adjacent R^1 groups together form (3-6C)alkylene, (2-4C)alkylene-O- or -O-(1-4C)alkylene)-O-; wherein each alkyl, alkenyl or cycloalkyl group is optionally substituted with from 1 to 5 fluorine atoms;

each of R^{1a}, R^{1b}, R^{1c}, R^{1d}, R^{1e} and R^{1f} is independently hydrogen or (1-4C)alkyl;

a is 0 or an integer of from 1 to 3;

Ar^2 represents a phenyl, (5-6C)cycloalkyl, (4-5C)heteroaryl or (4-5C)heterocyclyl group wherein the (4-5C)heteroaryl or (4-5C)heterocyclyl group contains one ring heteroatom selected from oxygen, nitrogen and sulfur;

each R^2 represents an optional substituent on Ar^2 that is independently selected from the group consisting of (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, $-OR^{2a}$, $-SR^{2b}$, $-S(O)R^{2c}$, $-S(O)_2R^{2d}$, and $-NR^{2e}R^{2f}$; or two adjacent R^2 groups together form (3-6C)alkylene, (2-4C)alkylene-O- or -O-(1-

4C)alkylene)-O-; wherein each alkyl, alkenyl or cycloalkyl group is optionally substituted with from 1 to 5 fluorine atoms;

each of R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{2e} and R^{2f} is independently hydrogen or (1-4C)alkyl;

b is 0 or an integer of from 1 to 3;

E is CN or $C(O)NW^aW^b$;

each of W^a and W^b is independently selected from hydrogen and (1-4C)alkyl, or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, morpholin-4-yl or thiomorpholin-4-yl group;

c is 0 or an integer of from 1 to 4;

each R^3 is a substituent on carbon independently selected from the group consisting of (1-4C)alkyl and fluoro, wherein each alkyl group is optionally substituted with from 1 to 5 fluorine atoms;

z is 1 or 2, the atom bearing the group E being attached to the ring containing the nitrogen atom at the 2- or 3-position with respect to the nitrogen atom;

R^4 is a divalent group of the formula:

$$-(R^{4a})_d-(A^1)_e-(R^{4b})_f-Q-(R^{4c})_g-(A^2)_h-(R^{4d})_i-$$

wherein

d, e, f, g, h and i are each independently selected from 0 and 1;

R^{4a}, R^{4b}, R^{4c} and R^{4d} are each independently selected from the group consisting of (1-10C)alkylene, (2-10C)alkenylene and (2-10C)alkynylene wherein each alkylene, alkenylene or alkynylene group is unsubstituted or substituted with from 1 to 5 substituents independently selected from the group consisting of (1-4C)alkyl, fluoro, hydroxy, phenyl and phenyl(1-4C)-alkyl;

A^1 and A^2 are each independently selected from (3-7C)cycloalkylene, (6-10C)arylene, (2-9C)heteroarylene and (3-6C)heterocyclene; wherein each cycloalkylene is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl and each arylene, heteroarylene or heterocyclene group is unsubstituted or substituted with from 1 to 4 substituents independently selected from the group consisting of halogen, (1-4C)alkyl and (1-4C)alkoxy;

Q is selected from the group consisting of a bond, -O-, -C(O)O-, -OC(O)-, -S-, -S(O)-, $-S(O)_2-$, $-N(Q^a)C(O)-$, $-C(O)N(Q^b)-$, $-N(Q^c)S(O)_2-$, $-S(O)_2N(Q^d)-$, $-N(Q^e)C(O)N(Q^f)-$, $-N(Q^g)S(O)_2N(Q^h)-$, $-OC(O)N(Q^i)-$ and $-N(Q^j)C(O)O-$;

Q^a, Q^b, Q^c, Q^d, Q^e, Q^f, Q^g, Q^h, Q^i and Q^j are each independently selected from the group consisting of hydrogen, (1-6C)alkyl, A^3 and (1-4C)alkylene-A^4; wherein the alkyl group is unsubstituted or substituted with from 1 to 3 substituents independently selected from fluoro, hydroxy and (1-4C)alkoxy; or together with the nitrogen atom and the group R^{4b} or R^{4c} to which they are attached, form a 4-6 membered azacycloalkylene group;

A^3 and A^4 are each independently selected from (3-6C)cycloalkyl, (6-10C)aryl, (2-9C)heteroaryl and (3-6C)heterocyclyl; wherein each cycloalkyl is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl and each aryl, heteroaryl or heterocyclyl group is unsubstituted or substituted with from 1 to 4 substituents independently selected from the group consisting of halogen, (1-4C)alkyl and (1-4C)alkoxy;

provided that the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is in the range of from 4 to 14;

R^5 represents hydrogen or (1-4C)alkyl;

R^6 is $-NR^{6a}CR^{6b}(O)$ or $-CR^{6c}R^{6d}OR^{6e}$ and R^7 is hydrogen, or R^6 and R^7 together form $-NR^{7a}C(O)-CR^{7b}=CR^{7c}-$, $-CR^{7d}=CR^{7e}-C(O)-NR^{7f}-$, $-NR^{7g}C(O)-CR^{7h}R^{7i}-CR^{7j}R^{7k}-$ or $-CR^{7l}R^{7m}-CR^{7n}R^{7o}-C(O)-NR^{7p}-$;

each of R^{6a}, R^{6b}, R^{6c}, R^{6d} and R^{6e} is independently hydrogen or (1-4C)alkyl; and

each of R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{7g}, R^{7h}, R^{7i}, R^{7j}, R^{7k}, R^{7l}, R^{7m}, R^{7n}, R^{7o} and R^{7p} is independently hydrogen or (1-4C)alkyl;

or a pharmaceutically-acceptable salt or solvate or stereoisomer thereof.

31. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of any one of Claims 1, 18, 19, 20 or 30.

32. (Withdrawn) The pharmaceutical composition of Claim 31, wherein the composition further comprises a therapeutically effective amount of a steroidal anti-inflammatory agent.

33. (Withdrawn) The pharmaceutical composition of Claim 31, wherein the composition further comprises a therapeutically effective amount of a PDE_4 inhibitor.

34. (Withdrawn) A method for treating a pulmonary disorder, the method comprising administering to a patient in need of treatment a therapeutically effective amount of a compound of any one of Claims 1, 18, 19, 20 or 30.

35. (Withdrawn) A method of providing bronchodilation in a patient, the method comprising administering to a patient requiring bronchodilation a therapeutically effective amount of a compound of any one of Claims 1, 18, 19, 20 or 30.

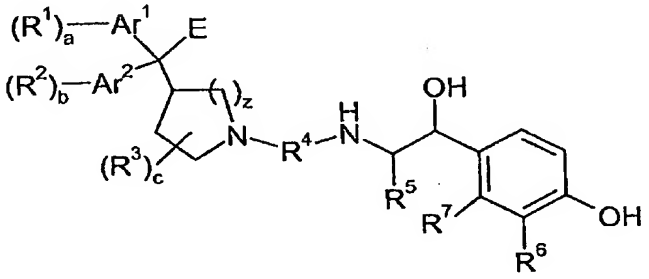
36. (Withdrawn) A method of treating chronic obstructive pulmonary disease or asthma, the method comprising administering to a patient in need of treatment a therapeutically effective amount of a compound of any one of Claims 1, 18, 19, 20 or 30.

37. (Withdrawn) A method of studying a biological system or sample comprising a muscarinic receptor or a β_2 adrenergic receptor, the method comprising:

(a) contacting the biological system or sample with a compound of Claim 1; and

(b) determining the effects caused by the compound of Claim 1 on the biological system or sample.

38. (Original) A process for preparing a compound of formula I:



I

wherein:

Ar^1 represents phenyl, (3-6C)cycloalkyl, (3-5C)heteroaryl or (3-5C)heterocyclyl; wherein the heteroaryl and heterocyclyl groups contain 1 or 2 ring heteroatoms selected independently from oxygen, nitrogen and sulfur;

a is 0 or an integer from 1 to 3;

each R^1 is selected independently from (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, $-OR^{1a}$, $-SR^{1b}$, $-S(O)R^{1c}$, $-S(O)_2R^{1d}$, $-NR^{1e}R^{1f}$ and $-C(O)OR^{1g}$; or two adjacent R^1 groups are joined together to form (3-6C)alkylene, (2-4C)alkylene-O- or -O-(1-4C)alkylene)-O-;

each of R^{1a}, R^{1b}, R^{1c}, R^{1d}, R^{1e}, R^{1f} and R^{1g} is independently hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl;

Ar^2 represents phenyl, (3-6C)cycloalkyl, (3-5C)heteroaryl or (3-5C)heterocyclyl; wherein the heteroaryl and heterocyclyl group contain 1 or 2 ring heteroatoms selected independently from oxygen, nitrogen and sulfur;

b is 0 or an integer of from 1 to 3;

each R^2 is selected independently from (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, $-OR^{2a}$, $-SR^{2b}$, $-S(O)R^{2c}$, $-S(O)_2R^{2d}$, $-NR^{2e}R^{2f}$ and $-C(O)OR^{2g}$; or two adjacent R^2 groups are joined together to form (3-6C)alkylene, (2-4C)alkylene-O- or -O-(1-4C)alkylene)-O-;

each of R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{2e}, R^{2f} and R^{2g} is independently hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl;

E is –CN, -C(O)N$W^a W^b$ or –C(O)OW^c;

W^a and W^b are selected independently from hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl, or together with the nitrogen atom to which they are attached, W^a and W^b form a pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, morpholin-4-yl or thiomorpholin-4-yl group; or W^a and one R^1 are joined to form a covalent bond;

W^c is hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl;

c is 0 or an integer of from 1 to 4;

each R^3 is independently selected from (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (3-6C)cycloalkyl, cyano, halo, -OR^{3a}, -SR^{3b}, -S(O)R^{3c}, -S(O)$_2$$R^{3d}$ and –N$R^{3e}R^{3f}$ and -C(O)OR^{3g}; or two R^3 groups are joined to form (1-3C)alkylene, (2-3C)alkenylene or oxiran-2,3-diyl;

each of R^{3a}, R^{3b}, R^{3c}, R^{3d}, R^{3e}, R^{3f} and R^{3g} is independently hydrogen, (1-4C)alkyl or phenyl-(1-4C)alkyl;

z is 1 or 2;

R^4 is a divalent group of the formula:

$$-(R^{4a})_d-(A^1)_e-(R^{4b})_f-Q-(R^{4c})_g-(A^2)_h-(R^{4d})_i-$$

wherein

d, e, f, g, h and i are each independently selected from 0 and 1;

R^{4a}, R^{4b}, R^{4c} and R^{4d} are each independently selected from (1-10C)alkylene, (2-10C)alkenylene and (2-10C)alkynylene, wherein each alkylene, alkenylene or alkynylene group is unsubstituted or substituted with from 1 to 5 substituents independently selected from (1-4C)alkyl, fluoro, hydroxy, phenyl and phenyl-(1-4C)alkyl;

A^1 and A^2 are each independently selected from (3-7C)cycloalkylene, (6-10C)arylene, -O-(6-10C)arylene, (6-10C)arylene-O-, (2-9C)heteroarylene, -O-(2-9C)heteroarylene, (2-9C)heteroarylene-O- and (3-6C)heterocyclene, wherein each cycloalkylene is unsubstituted or substituted with from 1 to 4 substitutents selected

independently from (1-4C)alkyl, and each arylene, heteroarylene or heterocyclene group is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl, (1-4C)alkoxy, –S-(1-4C)alkyl, -S(O)-(1-4C)alkyl, -$S(O)_2$-(1-4C)alkyl, -C(O)O(1-4C)alkyl, carboxy, cyano, hydroxy, nitro, trifluoromethyl and trifluoromethoxy;

Q is selected from a bond, -O-, -C(O)O-, -OC(O)-, -S-, -S(O)-, -$S(O)_2$-, -$N(Q^a)C(O)$-, -$C(O)N(Q^b)$-, -$N(Q^c)S(O)_2$-, -$S(O)_2N(Q^d)$-, -$N(Q^e)C(O)N(Q^f)$-, -$N(Q^g)S(O)_2N(Q^h)$-, -$OC(O)N(Q^i)$-, -$N(Q^j)C(O)O$- and –$N(Q^k)$;

Q^a, Q^b, Q^c, Q^d, Q^e, Q^f, Q^g, Q^h, Q^i, Q^j and Q^k are each independently selected from hydrogen, (1-6C)alkyl, A^3 and (1-4C)alkylene-A^4, wherein the alkyl group is unsubstituted or substituted with from 1 to 3 substituents independently selected from fluoro, hydroxy and (1-4C)alkoxy; or together with the nitrogen atom and the group R^{4b} or R^{4c} to which they are attached, form a 4-6 membered azacycloalkylene group;

A^3 and A^4 are each independently selected from (3-6C)cycloalkyl, (6-10C)aryl, (2-9C)heteroaryl and (3-6C)heterocyclyl, wherein each cycloalkyl is unsubstituted or substituted with from 1 to 4 substitutents selected independently from (1-4C)alkyl and each aryl, heteroaryl or heterocyclyl group is unsubstituted or substituted with from 1 to 4 substituents independently selected from halo, (1-4C)alkyl and (1-4C)alkoxy;

provided that the number of contiguous atoms in the shortest chain between the two nitrogen atoms to which R^4 is attached is in the range of from 4 to 16;

R^5 represents hydrogen or (1-4C)alkyl;

R^6 is -$NR^{6a}CR^{6b}(O)$ or -$CR^{6c}R^{6d}OR^{6e}$ and R^7 is hydrogen; or R^6 and R^7 together form -$NR^{7a}C(O)$-CR^{7b}=CR^{7c}- , -CR^{7d}=CR^{7e}-C(O)-NR^{7f}-, -$NR^{7g}C(O)$-$CR^{7h}R^{7i}$-$CR^{7j}R^{7k}$- or -$CR^{7l}R^{7m}$-$CR^{7n}R^{7o}$- C(O) -NR^{7p}-;

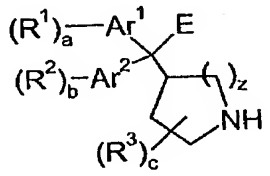
each of R^{6a}, R^{6b}, R^{6c}, R^{6d} and R^{6e} is independently hydrogen or (1-4C)alkyl; and

each of R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{7g}, R^{7h}, R^{7i}, R^{7j}, R^{7k}, R^{7l}, R^{7m}, R^{7n}, R^{7o} and R^{7p} is independently hydrogen or (1-4C)alkyl;

wherein each alkyl, alkenyl, alkylene and cycloalkyl group in R^1, R^{1a-g}, R^2, R^{2a-g}, R^3, R^{3a-g}, W^{a-c} is optionally substituted with from 1 to 5 fluoro substituents;

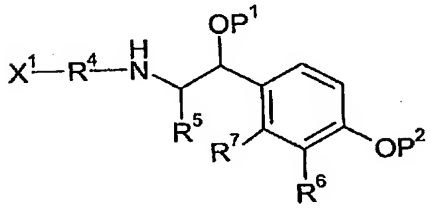
or a stereoisomer thereof; the process comprising:

(a) reacting a compound of formula 1:



1

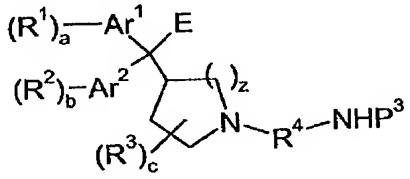
or a salt thereof; with a compound of formula 2:



2

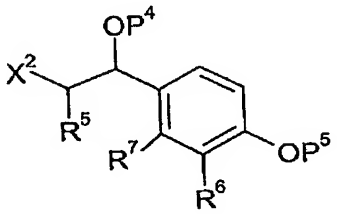
wherein X^1 represents a leaving group, and P^1 and P^2 each independently represent hydrogen or a hydroxyl-protecting group;

(b) reacting a compound of formula 3:



3

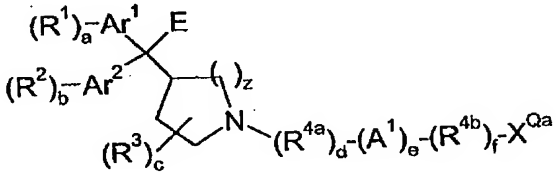
or salt thereof; wherein P^3 represents hydrogen or an amino-protecting group, with a compound of formula 4:



4

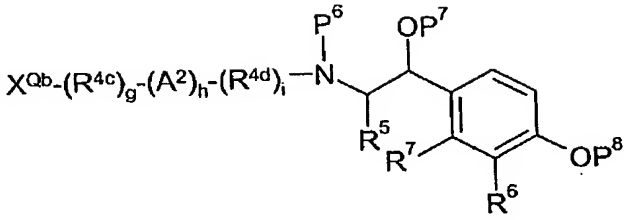
wherein X^2 represents a leaving group, and P^4 and P^5 each independently represent hydrogen or a hydroxyl-protecting group;

(c) coupling a compound of formula 5:



5

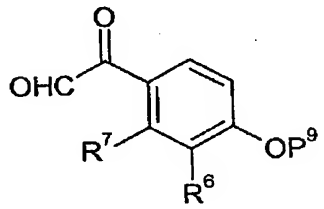
with a compound of formula 6:



6

wherein X^{Qa} and X^{Qb} each independently represent functional groups that couple to form a group Q, P^6 represents hydrogen or an amino-protecting group; and P^7 and P^8 each independently represent hydrogen or a hydroxyl-protecting group;

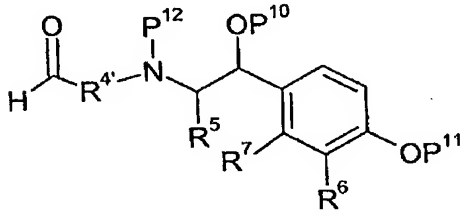
(d) for a compound of formula I wherein R^5 represents hydrogen, reacting a compound of formula 3 with a compound of formula 7:



7

or a hydrate thereof (e.g., a glyoxal), wherein P^9 represents hydrogen or a hydroxyl-protecting group, in the presence of a reducing agent;

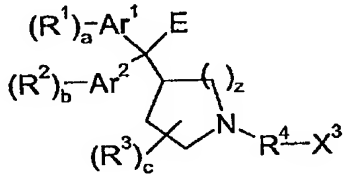
(e) reacting a compound of formula **1** with a compound of formula **8**:



8

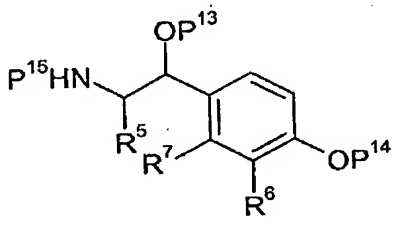
or a hydrate thereof, in the presence of a reducing agent, wherein P^{10} and P^{11} each independently represent hydrogen or a hydroxyl-protecting group; P^{12} represents hydrogen or an amino-protecting group; and $R^{4'}$ represents a residue that, together with the carbon to which it is attached, affords a group R^4 upon completion of the reaction;

(f) reacting a compound of formula **9**:



9

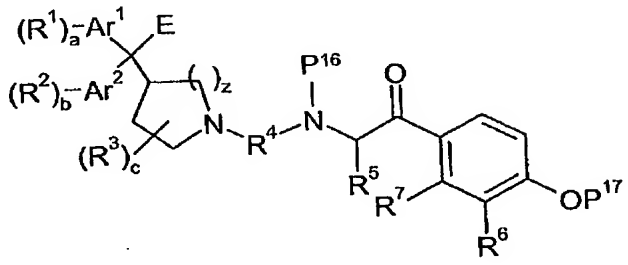
wherein X^3 represents a leaving group, with a compound of formula **10**:



10

wherein P^{13} and P^{14} each independently represent hydrogen or a hydroxyl-protecting group, and P^{15} represents hydrogen or an amino-protecting group;

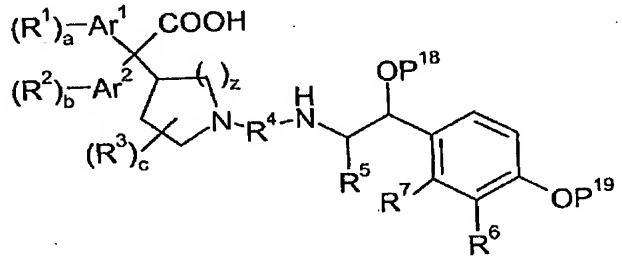
(g) reacting a compound of formula **11**:



11

with a reducing agent; wherein P^{16} represents hydrogen or an amino-protecting group; and P^{17} represents hydrogen or a hydroxyl-protecting group;

(h) for a compound of formula I in which E represents $C(O)NW^aW^b$, reacting a compound of formula **12**:



12

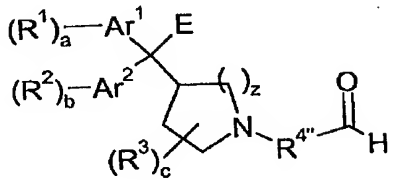
wherein P^{18} and P^{19} each represents hydrogen or a hydroxyl-protecting group, with a compound of formula **13**:

HNW^aW^b

13

or

(i) reacting a compound of formula **14**:



14

or a hydrate thereof; wherein $R^{4''}$ represents a residue that, together with the carbon to which it is attached, affords an R^4 group upon completion of the reaction; with a compound of formula **10** in the presence of a reducing agent;

and then removing any protecting group P^1, P^2, P^3, P^4, P^5, P^6, P^7, P^8, P^9, P^{10}, P^{11}, P^{12}, P^{13}, P^{14}, P^{15}, P^{16}, P^{17}, P^{18} or P^{19} to provide a compound of formula I.

39. (Original) The process of Claim 38, wherein the process further comprises forming a pharmaceutically acceptable salt of the compound of formula I.

40. Canceled.